

AMENDMENTS TO THE SPECIFICATION

Please amend the paragraph beginning at page 1, line 23 as follows:

Zinc finger proteins (ZFPs) are proteins that can bind to DNA in a sequence-specific manner. Zinc fingers were first identified in the transcription factor TFIIIA from the oocytes of the African clawed toad, *Xenopus laevis*. A single zinc finger domain of this class of ~~ZPFs~~ ZFPs is about 30 amino acids in length, and several structural studies have demonstrated that it contains a beta turn (containing the two invariant cysteine residues) and an alpha helix (containing the two invariant histidine residues), which are held in a particular conformation through coordination of a zinc atom by the two cysteines and the two histidines. This class of ZFPs is also known as C2H2 ZFPs. Additional classes of ZFPs have also been suggested. (See, e.g., Jiang et al. (1996) *J. Biol. Chem.* 271:10723-10730 for a discussion of Cys-Cys-His-Cys (C3H) ZPFs.) To date, over 10,000 zinc finger sequences have been identified in several thousand known or putative transcription factors. Zinc finger domains are involved not only in DNA recognition, but also in RNA binding and in protein-protein binding. Current estimates are that this class of molecules will constitute about 2% of all human genes.

Please amend the paragraph beginning at page 23, line 28 as follows:

Additional functional domains are disclosed, for example, in co-owned WO 00/41566. Common regulatory domains for addition to the ZFP include, e.g., effector domains from transcription factors (activators, repressors, co-activators, co-repressors), silencers, nuclear hormone receptors, oncogene transcription factors (e.g., myc, jun, fos, myb, max, mad, rel, ets, bcl, myb, mos family members etc.); DNA repair enzymes and their associated factors and modifiers; DNA rearrangement enzymes and their associated factors and modifiers; chromatin associated proteins and their modifiers (e.g., kinases, acetylases and deacetylases); and DNA modifying enzymes (e.g.,

methyltransferases, topoisomerases, helicases, ligases, kinases, phosphatases, polymerases, endonucleases) and their associated factors and modifiers.

Similarly, regulatory domains can be derived from DNA modifying enzymes (e.g., DNA methyltransferases, topoisomerases, helicases, ligases, kinases, phosphatases, polymerases) and their associated factors and modifiers. Helicases are reviewed in Matson et al., *Bioessays*, 16:13-22 (1994), and methyltransferases are described in Cheng, *Curr. Opin. Struct. Biol.* 5:4-10 (1995). Chromatin associated proteins and their modifiers (e.g., kinases, acetylases and deacetylases), such as histone deacetylase (Wolffe, *Science* 272:371-2 (1996)) are also useful as domains for addition to the ZFP of choice. In one preferred embodiment, the regulatory domain is a DNA methyl transferase that acts as a transcriptional repressor (see, e.g., Van den Wyngaert et al., *FEBS Lett.* 426:283-289 (1998); Flynn et al., *J. Mol. Biol.* 279:101-116 (1998); Okano et al., *Nucleic Acids Res.* 26:2536-2540 (1998); and Zardo & Caiafa, *J. Biol. Chem.* 273:16517-16520 (1998)). In another preferred embodiment, endonucleases such as FokI are used as transcriptional repressors, which act via gene cleavage (see, e.g., WO95/09233; and PCT/US94/01201). Further, insulator domains, chromatin remodeling proteins such as ISWI-containing domains and/or methyl binding domain proteins suitable for use in fusion molecules are described, for example, in ~~co-owned U.S. Patent applications 60/228,523; 60/228,618; 60/236,409; 60/236,884; 60/242,008 and 60/253,678.~~ WO 01/83793, WO 02/26959, WO 02/26960 and WO 02/44376.